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Remarks

In view of the foregoing amendments and the following remarks, Applicants respectfully request reconsideration and withdrawal of all outstanding objections and rejections and early allowance of the above-identified application.

Upon entry of the foregoing amendment, claims 12, 17-32 and 34-37 are pending in the application, with claims 12, 34 and 36 being the independent claims. New claims 34-37 are sought to be added.

These amendments are believed to introduce no new matter, and their entry is respectfully requested. Entry of these amendments is proper under 37 C.F.R. § 1.116 because they obviate one or more of the outstanding rejections and so place the pending claims in condition for allowance or, at the very least, in better form for appeal by reducing the of issues for review.

I. Rejection under 35 U.S.C. § 112

In the outstanding Office Action, the Examiner has maintained the outstanding rejection of claims 12-20 under 35 U.S.C. § 112, first paragraph. Applicants respectfully traverse this rejection.

First, contrary to the Examiner's statement on page 2 of the Office Action, the present invention is not a delivery system for delivery of antibodies to a patient. Rather, as noted previously, the present invention relates to a delivery system for a *supplement or supplements* to a patient. While one possible supplement is an antibody, the present invention is not limited to a delivery system for antibodies.

The inventive delivery system is based on a fibrin matrix formed by activation of fibrinogen (or fibrinopeptide A and/or fibrinopeptide B) component of the biocompatible tissue sealant composition. The presently claimed invention is premised, in part, on the discovery that a supplement(s) contained in such a fibrin matrix can be delivered to a predetermined area, such as the tissue of a patient, by release from this fibrin matrix when it is placed in the environment of use.

The present specification provides ample guidance to one skilled in the art to make and use the fibrin matrix employed in the inventive delivery system. For example, the present specification discloses the basic components of the biocompatible tissue sealant that forms the fibrin matrix (*see, e.g.*, page 37, line 23, to page 38, line 4). The present specification discloses how to incorporate a supplement into the biocompatible tissue sealant (*see, e.g.*, page 37, lines 5-15 and the Examples).

In addition, a number of examples are provided in the specification that show the inclusion in a biocompatible tissue sealant of various supplements from among the groups recited in the claims. These examples also show the delivery of the supplements from the fibrin matrix into the environment of use (*see, e.g.*, page 62, Example 4; page 69-70, Example 9; page 71-72, Example 10; page 83-91, Example 13; page 91-97, Example 14; page 98-99, Example 17, page 102-105, Example 19; page 117-118, Example 23; and page 118-119, Example 24).

Given this level of disclosure, the amount of experimentation required to practice the presently claimed invention is not excessive. Rather, the skilled worker need only select a given supplement (or supplements) for which delivery to a patient is desired and incorporate that into the biocompatible tissue sealant as described in the specification. The resulting

composition can then be assayed, for example according to any one of the methods disclosed in the present specification, for its efficacy as a delivery system for the supplement.

Moreover, the Examiner should note that if a particular supplement/tissue sealant composition does not exhibit the requisite release of the supplement into the environment of use, then such a composition would not be a "delivery system" and would therefore be outside the scope of the present claims.

The Examiner's comments concerning hypothetical compositions do not support the outstanding rejection and are not themselves supported by the evidence of record. For example, the comments concerning the behavior of an emulsified protein relative to that of an antibody solubilized in water are totally unsupported by the evidence of record. Moreover, it should be emphasized that simply because certain supplements may not work in certain embodiments of the claimed invention (a point Applicants do *not* concede), such does not render the specification non-enabling.

Finally, Applicants disagree with the Examiner's statements concerning the alleged lack of support for antibodies in the parent applications. In particular, the Examiner's attention is respectfully drawn to the disclosure at page 21, line 24 to page 22, line 11 of the specification of Appl. No. 07/798,919, filed November 27, 1991, where it is noted that antibodies may be used as the supplement in the inventive delivery system. Thus, contrary to the Examiner's assertion, claims reciting "antibodies" as a supplement are entitled to at least benefit of the filing date of Appl. No. 07/798,919.

For these reasons, withdrawal of the outstanding rejection is respectfully requested.

II. Rejections under 35 U.S.C. § 102

A. Cadoni et al.

The Examiner has rejected claims 12-15, 17-20 and 29 under 35 U.S.C. § 102(b) as allegedly anticipated by Cadoni *et al.*, *Endoscopy 22*:194-195 (1990). Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Cadoni *et al.* do not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

As presently claimed in claim 36, the inventive delivery system comprises a biocompatible tissue sealant and at least one protein supplement for delivery. As conceded by the Examiner in the outstanding Office Action, Cadoni does not teach or suggest a fibrin matrix containing such a supplement.

Moreover, there is no teaching or suggestion in the cited reference of the sustained release of an effective amount of the supplement, as in the invention claimed in all of claims 12, 34 and 36. Indeed, although Cadoni *et al.* state the an antibiotic was released from a tissue sealant composition, the reference also teaches that it was necessary to wash the site with an antibiotic solution prior to application of the tissue sealant and that it was necessary to administer additional broad-spectrum antibiotics. In view of these teachings, it is clear that the tissue sealant used by Cadoni *et al.* did *not* release sufficient amounts of antibiotic to be effective.

Accordingly, the cited reference fails to teach inclusion of a supplement above its solubility limit, as presently claimed in claims 12 and 34, or the inclusion of a protein supplement, as claimed in claim 36, or the sustained release of an effective amount of the supplement into the environment of use. Withdrawal of the outstanding rejection is therefore requested.

B. Sakurai et al.

The Examiner has rejected claims 12-15, 17-20 and 29-33 under 35 U.S.C. § 102(b) as allegedly anticipated by Sakurai *et al.*, *J. Controlled Release 18*:39-44 (1992). Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Sakurai *et al.* do not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, Applicants note that, contrary to the Examiner's allegations, the presently claimed invention is supported by Appl. No. 07/798,919, which was filed November 27, 1991. Accordingly, Sakurai *et al.* is not even prior art against (at least some of) the presently pending claims. The Examiner's attention is respectfully drawn to the following exemplary portions of the present specification: page 21, line 10, to page 22, line 5; page 40, lines 23-26; page 41, lines 8-26; and page 46, lines 1-21; page 92, line 16, to page 93, line 21; and page 97, line 16, to page 98, line 9 (claims 12, 17-20, 24-26 and 33); and page 33, lines 6-11; and page 36, line 25, to page 37, line 3 (claims 30-32).

Thus, contrary to the Examiner's allegations, at least pending claims 12, 17-20, 24-26 and 30-33 are fully supported by prior Appl. No. 07/798,919, filed November 27, 1991. Conversely, Sakurai *et al.* was published in 1992. Accordingly, Sakurai *et al.* is not prior art against any of these claims and any rejection thereof based on Sakurai *et al.* must be withdrawn.

Finally, with respect to claims 34 and 36 (and those claims dependent thereon), as conceded by the Examiner in characterizing the reference, Sakurai *et al.* do not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of a particular supplement to a patient. Applicants note that the cited reference itself does not support the Examiner's allegation of sustained local release. Withdrawal of the outstanding rejection is therefore respectfully requested.

C. Greco et al.

The Examiner has rejected claims 12-20 and 29-33 under 35 U.S.C. § 102(b) as allegedly anticipated by Greco *et al.*, *J. Biomedical Materials Res. 25*:39-51 (1991). Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Greco *et al.* do not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, Applicants note that, contrary to the Examiner's allegations, the presently claimed invention is supported by Appl. No. 07/798,919, which was filed November 27, 1991.

Accordingly, Greco *et al.* is not even prior art against (at least some of) the presently pending claims. The Examiner's attention is respectfully drawn to the following exemplary portions of the present specification: page 21, line 10, to page 22, line 5; page 40, lines 23-26; page 41, lines 8-26; and page 46, lines 1-21; page 92, line 16, to page 93, line 21; and page 97, line 16, to page 98, line 9 (claims 12, 17-20, 24-26 and 33); and page 33, lines 6-11; and page 36, line 25, to page 37, line 3 (claims 30-32).

Thus, contrary to the Examiner's allegations, at least pending claims 12, 17-20, 24-26 and 30-33 are fully supported by prior Appl. No. 07/798,919, filed November 27, 1991. Conversely, Greco *et al.* was published in 1991. Accordingly, any rejection of claims 12, 17-20, 24-26 and 30-33 under 35 U.S.C. § 102(b) must be withdrawn.

Finally, with respect to claims 34 and 36 (and those claims dependent thereon), as conceded by the Examiner in characterizing the reference, Greco *et al.* do not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of a particular supplement to a patient. Applicants note that the cited reference itself does not support the Examiner's allegation of sustained local release. Withdrawal of the outstanding rejection is therefore respectfully requested.

D. JP 60-204725

The Examiner has rejected claims 12-15, 17-20, 24 and 29-33 under 35 U.S.C. § 102(b) as allegedly anticipated by the English language abstract of JP 60-204725. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in

an amount greater than that which is soluble in the fibrin matrix. The cited reference does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit. There is also no teaching or suggestion of the supplement being released from the fibrin matrix, much less for a sustained period as presently claimed.

Finally, with respect to claims 34 and 36 (and those claims dependent thereon), as conceded by the Examiner in characterizing the reference, the English language abstract of JP 60-204725 does not teach or suggest the inclusion of any of the recited supplements in a fibrin matrix, much less the presently claimed invention which provides sustained delivery of a particular supplement to a patient. Applicants note that the cited reference itself does not support the Examiner's allegation of sustained local release -- support for such an allegation can only be found in the present specification. Withdrawal of the outstanding rejection is therefore respectfully requested.

E. Khadem et al.

The Examiner has rejected claims 12-15, 17-20 and 29-33 under 35 U.S.C. § 102(e) as allegedly anticipated by Khadem *et al.*, U.S. Patent No. 5,552,452. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Khadem *et al.* do not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, Applicants note that, contrary to the Examiner's allegations, the presently claimed invention is supported by Appl. No. 07/798,919, which was filed November 27, 1991. Accordingly, Khadem *et al.* is not even prior art against (at least some of) the presently pending claims. The Examiner's attention is respectfully drawn to the following exemplary portions of the present specification: page 21, line 10, to page 22, line 5; page 40, lines 23-26; page 41, lines 8-26; and page 46, lines 1-21; page 92, line 16, to page 93, line 21; and page 97, line 16, to page 98, line 9 (claims 12, 17-20, 24-26 and 33); and page 33, lines 6-11; and page 36, line 25, to page 37, line 3 (claims 30-32).

Thus, contrary to the Examiner's allegations, at least pending claims 12, 17-20, 24-26 and 30-33 are fully supported by prior Appl. No. 07/798,919, filed November 27, 1991. Accordingly, Khadem *et al.* is not prior art against any of these claims and any rejection thereof based on Khadem *et al.* must be withdrawn.

Finally, with respect to claims 34 and 36 (and those claims dependent thereon), as conceded by the Examiner in characterizing the reference, Khadem *et al.* do not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of these supplements to a patient. Applicants note that the cited reference itself does not support the Examiner's allegation of sustained local release. Withdrawal of the outstanding rejection is therefore respectfully requested.

F. Lontz

The Examiner has rejected claims 12-20 and 30-33 under 35 U.S.C. § 102(e) as allegedly anticipated by Lontz, U.S. Patent No. 5,420,250. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Lontz does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, Applicants note that, contrary to the Examiner's allegations, the presently claimed invention is supported by Appl. No. 07/798,919, which was filed November 27, 1991. Accordingly, Lontz is not even prior art against (at least some of) the presently pending claims. The Examiner's attention is respectfully drawn to the following exemplary portions of the present specification: page 21, line 10, to page 22, line 5; page 40, lines 23-26; page 41, lines 8-26; and page 46, lines 1-21; page 92, line 16, to page 93, line 21; and page 97, line 16, to page 98, line 9 (claims 12, 17-20, 24-26 and 33); and page 33, lines 6-11; and page 36, line 25, to page 37, line 3 (claims 30-32).

Thus, contrary to the Examiner's allegations, at least pending claims 12, 17-20, 24-26 and 30-33 are fully supported by prior Appl. No. 07/798,919, filed November 27, 1991. Accordingly, Lontz is not prior art against any of these claims and any rejection thereof based on Lontz must be withdrawn.

Finally, with respect to claims 34 and 36 (and those claims dependent thereon), Lontz does not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of these supplements to a patient. Applicants note that the cited reference itself does not support the Examiner's allegation of sustained local release. Withdrawal of the outstanding rejection is therefore respectfully requested.

G. Stroetmann

The Examiner has rejected claims 12-20 and 29-33 under 35 U.S.C. § 102(b) as allegedly anticipated by Stroetmann, U.S. Patent No. 4,427,651. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Stroetmann does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

With respect to claims 34 and 36 (and those claims dependent thereon), Streotmann does not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of these supplements to a patient. Withdrawal of the outstanding rejection is therefore requested.

H. Luck

The Examiner has rejected claims 12-20, 24 and 30-33 under 35 U.S.C. § 102(b) as allegedly anticipated by Luck, U.S. Patent No. 4,619,913. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Luck does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Additionally, with respect to claims 34 and 36 (and those claims dependent thereon), Luck does not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of these supplements to a patient. Withdrawal of the outstanding rejection is therefore requested.

I. Wahlig

The Examiner has rejected claims 12-20 and 29-33 under 35 U.S.C. § 102(b) as allegedly anticipated by Wahlig, U.S. Patent No. 4,853,225. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Wahlig does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, with respect to claims 34 and 36 (and those claims dependent thereon), Wahlig does not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of these supplements to a patient. Withdrawal of the outstanding rejection is therefore requested.

J. Juergensen

The Examiner has rejected claims 12-20, 25 and 30-33 under 35 U.S.C. § 102(e) as allegedly anticipated by Juergensen, U.S. Patent No. 5,549,904. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Juergensen does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, Applicants note that, contrary to the Examiner's allegations, the presently claimed invention is supported by Appl. No. 07/798,919, which was filed November 27, 1991. Accordingly, Juergensen is not even prior art against (at least some of) the presently pending claims. The Examiner's attention is respectfully drawn to the following exemplary portions of the present specification: page 21, line 10, to page 22, line 5; page 40, lines 23-26; page 41, lines 8-26; and page 46, lines 1-21; page 92, line 16, to page 93, line 21; and page 97, line 16, to page 98, line 9 (claims 12, 17-20, 24-26 and 33); and page 33, lines 6-11; and page 36, line 25, to page 37, line 3 (claims 30-32).

Thus, contrary to the Examiner's allegations, at least pending claims 12, 17-20, 24-26 and 30-33 are fully supported by prior Appl. No. 07/798,919, filed November 27, 1991. Accordingly, Juergensen is not prior art against any of these claims and any rejection thereof based on Juergensen must be withdrawn.

Finally, with respect to claims 34 and 36 (and those claims dependent thereon), as conceded by the Examiner in characterizing the reference, Juergensen does not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of a particular supplement to a patient. Applicants note that the cited reference itself does not support the Examiner's allegation of sustained local release. Withdrawal of the outstanding rejection is therefore respectfully requested.

K. Marx

The Examiner has rejected claims 12-20 and 24-33 under 35 U.S.C. § 102(e) as allegedly anticipated by Marx, U.S. Patent No. 5,607,694. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Marx does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, Applicants note that, contrary to the Examiner's allegations, the presently claimed invention is supported by Appl. No. 07/798,919, which was filed November 27, 1991. Accordingly, Marx is not even prior art against (at least some of) the presently pending claims. The Examiner's attention is respectfully drawn to the following exemplary portions of the present specification: page 21, line 10, to page 22, line 5; page 40, lines 23-26; page 41, lines 8-26; and page 46, lines 1-21; page 92, line 16, to page 93, line 21; and page 97, line 16, to page 98, line 9 (claims 12, 17-20, 24-26 and 33); and page 33, lines 6-11; and page 36, line 25, to page 37, line 3 (claims 30-32).

Thus, contrary to the Examiner's allegations, at least pending claims 12, 17-20, 24-26 and 30-33 are fully supported by prior Appl. No. 07/798,919, filed November 27, 1991. Accordingly, Marx is not prior art against any of these claims and any rejection thereof based on Marx must be withdrawn.

Additionally, with respect to claims 34 and 36 (and those claims dependent thereon), Marx does not teach or suggest a fibrin sealant delivery system for any of the recited

supplements, much less the presently claimed invention which provides sustained delivery of a particular supplement to a patient. Withdrawal of the outstanding rejection is therefore respectfully requested.

L. Gristina

The Examiner has rejected claims 12-20, 25 and 30-33 under 35 U.S.C. § 102(e) as allegedly anticipated by Gristina, U.S. Patent No. 5,505,945. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. Gristina does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, Applicants note that, contrary to the Examiner's allegations, the presently claimed invention is supported by Appl. No. 07/798,919, which was filed November 27, 1991. Accordingly, Gristina is not even prior art against (at lest some of) the presently pending claims. The Examiner's attention is respectfully drawn to the following exemplary portions of the present specification: page 21, line 10, to page 22, line 5; page 40, lines 23-26; page 41, lines 8-26; and page 46, lines 1-21; page 92, line 16, to page 93, line 21; and page 97, line 16, to page 98, line 9 (claims 12, 17-20, 24-26 and 33); and page 33, lines 6-11; and page 36, line 25, to page 37, line 3 (claims 30-32).

Thus, contrary to the Examiner's allegations, at least pending claims 12, 17-20, 24-26 and 30-33 are fully supported by prior Appl. No. 07/798,919, filed November 27, 1991.

Accordingly, Gristina is not prior art against any of these claims and any rejection thereof based on that reference must be withdrawn.

Finally, with respect to claims 34 and 36 (and those claims dependent thereon), as conceded by the Examiner in characterizing the reference, Gristina does not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of a particular supplement to a patient. Applicants note that the cited reference itself does not support the Examiner's allegation of sustained local release. Withdrawal of the outstanding rejection is therefore respectfully requested.

M. WO 92/17206

The Examiner has rejected claims 12-20, 27 and 30-33 under 35 U.S.C. § 102(a) as allegedly anticipated by WO 92/17206. Applicants respectfully traverse this rejection.

As presently claimed in claims 12 and 34, the inventive delivery system comprises a biocompatible tissue sealant and at least one supplement, wherein the supplement is present in an amount greater than that which is soluble in the fibrin matrix. WO 92/17206 does not teach or suggest such a delivery system -- there is no teaching or suggestion in the reference of incorporating the supplement in the fibrin matrix above its solubility limit.

Moreover, Applicants note that, contrary to the Examiner's allegations, the presently claimed invention is supported by Appl. No. 07/798,919, which was filed November 27, 1991. Accordingly, WO 92/17206 is not even prior art against (at least some of) the presently pending claims. The Examiner's attention is respectfully drawn to the following exemplary portions of the present specification: page 21, line 10, to page 22, line 5; page 40, lines 23-26; page 41, lines 8-26; and page 46, lines 1-21; page 92, line 16, to page 93, line 21; and page

97, line 16, to page 98, line 9 (claims 12, 17-20, 24-26 and 33); and page 33, lines 6-11; and page 36, line 25, to page 37, line 3 (claims 30-32).

Thus, contrary to the Examiner's allegations, at least pending claims 12, 17-20, 24-26 and 30-33 are fully supported by prior Appl. No. 07/798,919, filed November 27, 1991. Accordingly, WO 92/17206 is not prior art against any of these claims and any rejection thereof based thereon must be withdrawn.

Finally, with respect to claims 34 and 36 (and those claims dependent thereon), as conceded by the Examiner in characterizing the reference, WO 92/17206 does not teach or suggest a delivery system for any of the recited supplements, much less the presently claimed invention which provides sustained delivery of a particular supplement to a patient. Applicants note that the cited reference itself does not support the Examiner's allegation of sustained local release. Withdrawal of the outstanding rejection is therefore respectfully requested.

III. Rejections under 35 U.S.C. § 103

A. Juergenson in view of Gerhart

The Examiner has rejected claim 26 under 35 U.S.C. § 103(a) as allegedly obvious over Juergenson as applied to claims 12-20, 25 and 30-33 above in view of Gerhart, U.S. Patent No. 5,364,839. Applicants respectfully traverse this rejection.

The deficiencies of Juergenson have been discussed above with respect to the rejection of claims 12-20, 25 and 30-33. Gerhart does not remedy those deficiencies. Moreover, Gerhart is not even prior art with respect to (at least some of) the pending claims. Withdrawal of the outstanding rejection is therefore requested.

B. Juergenson in view of Oppermann

The Examiner has rejected claim 12-20, 26 and 30-33 under 35 U.S.C. § 103(a) as allegedly obvious over Juergenson as applied to claims 12-20, 25 and 30-33 above in view of Oppermann, U.S. Patent No. 5,354,557. Applicants respectfully traverse this rejection.

The deficiencies of Juergenson have been discussed above with respect to the rejection of claims 12-20, 25 and 30-33. Oppermann does not remedy those deficiencies. Moreover, Oppermann is not even prior art with respect to (at least some of) the pending claims. Withdrawal of the outstanding rejection is therefore requested.

C. Weiner

The Examiner has rejected claims 12-20, 28 and 30-33 under 35 U.S.C. § 103(a) as allegedly obvious over Weiner, U.S. Patent No. 5,366,958. Applicants respectfully traverse this rejection.

As conceded by the Examiner, Weiner does not teach or suggest a fibrin matrix, but rather, lipid vesicles containing an oligonucleotide. Nevertheless, the Examiner has alleged that it would have been obvious to include such lipid vesicles in fibrin matrix implants.

This allegation, however, is not supported by any of the cited references. The Examiner is reminded that *all* limitations in a claim must be considered and found in the prior art to support the outstanding rejection. It is improper for the Examiner simply to allege the obviousness of a combination without citing prior art (or providing a declaration under 37 C.F.R. § 1.107) to support that combination. As no such citation is found in the present case, the outstanding rejection is untenable and should be withdrawn.

IV. Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn.

Applicants believe that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Respectfully submitted,

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